

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner  
 US Department of Commerce  
 United States Patent and Trademark  
 Office, PCT  
 2011 South Clark Place Room  
 CP2/5C24  
 Arlington, VA 22202  
 ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

|  |  |
|--|--|
| <b>Date of mailing (day/month/year)</b><br>30 January 2001 (30.01.01)        |  |
| <b>International application No.</b><br>PCT/GB00/02365                       | <b>Applicant's or agent's file reference</b><br>ML/P32329        |
| <b>International filing date (day/month/year)</b><br>16 June 2000 (16.06.00) | <b>Priority date (day/month/year)</b><br>16 June 1999 (16.06.99) |
| <b>Applicant</b><br>CAMILLERI, Patrick et al                                 |  |

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:  
 13 December 2000 (13.12.00)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



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|--|---|--|
| Applicant's or agent's file reference<br>ML/FR/P32329                                      | <b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) |  |
| International application No.<br>PCT/GB00/02365  | International filing date (day/month/year)<br>16/06/2000  | Priority date (day/month/year)<br>16/06/1999 |
| International Patent Classification (IPC) or national classification and IPC<br>C07C215/10 |   |  |
| Applicant<br>SMITHKLINE BEECHAM P.L.C.   |   |  |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

|   |  |
|---|--|
| Date of submission of the demand<br><br>13/12/2000  | Date of completion of this report<br><br>06.08.2001  |
| Name and mailing address of the international preliminary examining authority:<br><br> European Patent Office<br>D-80298 Munich<br>Tel. +49 89 2399 - 0 Tx: 523656 epmu d<br>Fax: +49 89 2399 - 4465 | Authorized officer<br><br>Herzog, A<br><br>Telephone No. +49 89 2399 8033<br> |

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/GB00/02365

**I. Basis of this report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, pages:**

1-11 as originally filed

**Claims, No.:**

1-20 as originally filed

**Drawings, sheets:**

1/3-3/3 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/GB00/02365

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 1-11,19.

because:

☒ the said international application, or the said claims Nos. 1-11,19 relate to the following subject matter which does not require an international preliminary examination (*specify*):  
**see separate sheet**

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)

Yes: Claims 1-20

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/GB00/02365

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|                               |      |        |              |
|-------------------------------|------|--------|--------------|
|                               | No:  | Claims |              |
| Inventive step (IS)           | Yes: | Claims | 2,15         |
|                               | No:  | Claims | 1,3-14,16-20 |
| Industrial applicability (IA) | Yes: | Claims | 12-18,20     |
|                               | No:  | Claims |              |

2. Citations and explanations  
**see separate sheet**

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:  
**see separate sheet**

**R Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

Claims 1-11 and 19 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

For the assessment of the present claims 1-11 and 19 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

**Re Item V**

**Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

D1: XP000749400 (Gao, X. et al., Gene Therapy, GB, Macmillan Press LTD., Basingstoke, vol. 2, no. 10 (1995), p. 710-722; ISSN: 0969-7128)

D2: XP000900923 (Pestman, J.M. et al., Langmuir, vol. 13 (1997), p. 6857-6860)

The present application relates to carbohydrate-based surfactant compounds (claims 12-18), a process for preparing said compounds (claim 20) as well as to their use for facilitating the transfer of polynucleotides such as DNA or RNA or an anti-infective compound into a prokaryotic or eukaryotic cell or organism (claims 1-11 and 19).

1. D1 discloses the use of cationic liposomes as a vehicle for human gene therapy

(cf. abstract).

D2 discloses non-ionic carbohydrate-based gemini surfactants the structure of which falls within the scope of formula (I) in present claim 1 (use claim), but not within the scope of present compound claims 12-18 (cf. D2, p. 6857, col. 2, Figure 1). A possible use of the surfactants for facilitating the transfer of polynucleotides into cells has not been mentioned in D2.

The subject-matter of present claims 1-20 thus seems to be new over the cited prior art.

- 2.1 The subject-matter of present claims 2 and 15 relates to carbohydrate-based surfactant compounds or the use thereof wherein the variables  $Y_1$  and  $Y_2$  represent a sugar (claim 15: glucitol). The examples in the description and Fig. 1 and 2 show the activity of different compounds wherein  $Y_1$  and  $Y_2$  represent glucose in open chain form (glucitol). No hint can be found in the available prior art that said compounds could be used as vector systems in gene therapy. The subject-matter of present claims 2 and 15 can thus be considered inventive.
- 2.2 The present application does not meet the requirements of Article 33(3) PCT, because the subject-matter of present claims 1, 3-14 and 16-20 does not involve an inventive step.

The expression "carbohydrate group" in the definition of the variables  $Y_1$  and  $Y_2$  in present claim 1 encompasses a huge amount of compounds or residues which are not likely to be suitable in the surfactants of the present invention, i.e. in surfactants used for facilitating the transfer of DNA or RNA polynucleotides into cells. Thus, not all compounds included in present claim 1 are able to solve the problem posed, contrary to the requirements of Article 33(3) PCT.

Since claims 3-14, 16-18 and 19 also encompass compounds or the use of compounds with carbohydrate groups other than sugars, these claims and thus also process claim 20 do not meet the requirements of Article 33(3) PCT either.

Moreover, it is observed that in all the examples in the specification,  $Y_1$  and  $Y_2$  represent a sugar residue. Residues other than sugars are thus not supported by the description and examples (Article 6 PCT).

3. Industrial applicability can be acknowledged for present claims 12-18 and 20.

**Re Item VIII**

**Certain observations on the international application**

1. In claim 15, it is not clear how the glucose residue is connected to the nitrogen atom (Article 6 PCT).
2. Claim 16 is formulated as an independent claim. However, the structure of formula (I) mentioned therein is not included in said claim (Article 6 PCT).  
The same objection applies to claim 17.
3. Claim 20 is not clear in that the expression "addition of carbohydrate groups at the amine ends of an alkyl diamine compound" does not tell anything about how said addition should be carried out or about the structure of the carbohydrate educt used to carry out the reaction (Article 6 PCT).
4. In Scheme 1 (page 5), it is not clear how the reaction with the compound  $\text{CH}_3(\text{CH}_2)_{14}\text{CHO}$  could lead to a compound with an alkyl residue  $\text{CH}_3(\text{CH}_2)_m-$  wherein  $m$  represents 11-17 (Article 6 PCT).



# PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

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|--|---|--|
| Applicant's or agent's fil reference<br><b>ML/P32329</b> | <b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as w ll as, wh re applicabl , item 5 below. |  |
| International application No.<br><b>PCT/GB 00/ 02365</b> | International filing date (day/month/year)<br><b>16/06/2000</b>   | (Earliest) Priority Date (day/month/year)<br><b>16/06/1999</b> |
| Applicant<br><b>SMITHKLINE BEECHAM P.L.C.</b>            |   |  |

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

### 1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

**POLYHYDROXY DIAMINE SURFACTANTS AND THEIR USE IN GENE TRANSFER**

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

**A. CLASSIFICATION OF SUBJECT MATTER**  
 IPC 7 C07C215/10 C12N15/87

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07C C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, CHEM ABS Data

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

| Category * | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No. |
|------------|---|-----------------------|
| A          | GAO X ET AL: "CATIONIC LIPOSOME-MEDIATED GENE TRANSFER"<br>GENE THERAPY, GB, MACMILLAN PRESS LTD., BASINGSTOKE,<br>vol. 2, no. 10,<br>1 December 1995 (1995-12-01), pages<br>710-722, XP000749400<br>ISSN: 0969-7128<br>cited in the application<br>the whole document<br>-----<br>-/-- | 1, 12                 |



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

\* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

27 September 2000

Date of mailing of the international search report

06/10/2000

Name and mailing address of the ISA

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Authorized officer

de Nooy, A

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No. |
|------------|---|-----------------------|
| A          | <p>J.M. PESTMAN ET AL.: "Nonionic<br/>bolaamphiphiles and gemini surfactants<br/>based on carbohydrates"<br/>LANGMUIR,<br/>vol. 13, 1997, pages 6857-6860,<br/>XP000900923<br/>cited in the application<br/>page 6857, figure 1<br/>_____</p> | 12                    |